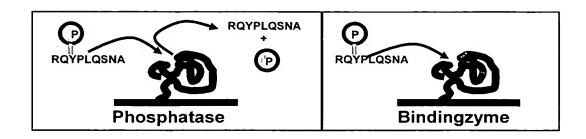
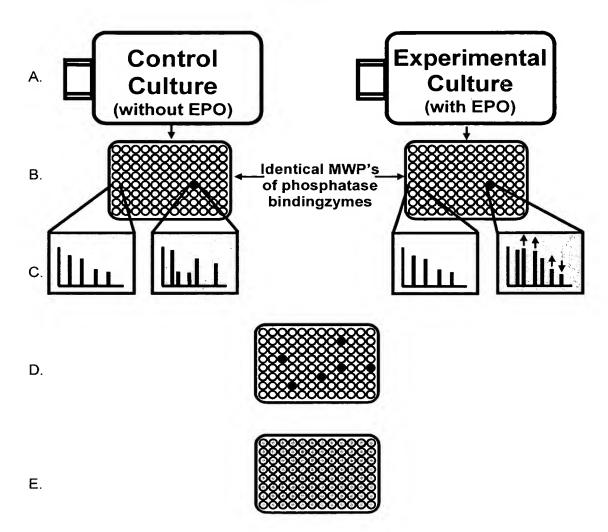
### FIGURE 1



#### FIGURE 2



# FIGURE 3A

	p			 pu	es.					 ს	tion								 Ľ					<u>.</u> =			<b>e</b>	<u>–</u>	_
Comment	Regulates T- and	B-cell signalling.	Can activate Src	family kinases and	inhibit JAK kinases	ביפט פרט	rir and acid	2000		Cancer Panel; C-	terminal prenylation	motif	Prenylated, All	affect	Jone Dance	Prenylated	adult & fetal heart		Substrates: EGFK 8. Shc	200	TOD signalling.	MAPK	<u> </u>	Variants exhibit	tissue-specific	expression.	Isoforms c, d are	candidates for the	Cancer Panel
Isoforms	-	7	က	•	4	Ø	b (Bs)	c, (Bf)	-	-		7	-	7				-	7	က	_	7	_	Ø	Q	ပ	ъ	ပ	ס
Aliases		LCA. LY5. B220.	CD45 T200 GP180				HAAP, MGC3499		HH13, OV-1, PRL2,	HH7-2, PRL-2,	PTP4A, HU-PP-1,	PTPCAAX2, ptp- IV1a, ptp-IV1b	PRL3, PRL-3, PRL-	<b>C</b>	HH72, PRL1, PRL-1,	PTPCAAX1,	PTPI A		PIPI, ICPIP, IC-	717, 105657	LPTP, HEPTP,	PTPNI, BPTP-4, LC-	PTP			PTPU2, GLEPP1,	PTP-U2		
RefSeq ID	NM 002838	NM 080921	NM 080922		NM 080923	NM 177554	00200 WN	NM 004300	NM 003479	NM 080391		NM 080392	NM 032611	007079 MN		NM 003463	NM 014241	NM 002828	NM 080422	NM 080423	NM 002832	NM 080588	NM 080589	NM 030667	NM 002848	NM 030669	NM 030668	NM 030671	NM 030670
Shortest		;	34				20				82		077	74 <u>7</u>		173	288	3	353			360				277	ò		
Peptide Length	1304	1143	1256		34	70	158	158	167	167		82	173	148		173	288	415	387	353	360	388	360	1216	1188	405	377	405	377
Variant	-	2	က		4	_	2	က	<del>-</del>	7		က	_	2				-	2	က	-	2	က	<del></del>	2	က	4	വ	9
Gene ID			PTPRC				ACP1				PTP4A2		4	7174A3		PTP4A1	D IOTO	<b>S</b> =	PTPN2			PTPN7				Cagta			
Bindingzyme			τ-				2				က		•	4		2	ď	<b>&gt;</b>	7			80				c	n		

FIGURE 3B

Bindingzyme	Gene ID	Variant	Peptide Length	Shortest	RefSeq ID	Aliases	Isoforms	Comment
10	PTEN		403	403	NM 000314	BZS, MHAM, TEP1, MMAC1, PTEN1		Cancer Panel
7	PTPRR	- 2	657 412	412	NM 002849 NM 130846	PTPRQ, EC-PTP, PCPTP1, PTP-SL, PTPRR7	- 0	Neuronal growth and differentiation
12	PTPN1		435	435	NM_002827	PTP18		Diabetes
13	PTPN11	-	593	460	NM_002834	CFC, NS1, SHP2, BPTP3, PTP2C, SHP-2, PTP-1D, SH- PTP2, SH-PTP3	<del>-</del>	Mutations associated w/Noonan syndrome.
41	PTPN18	7	460 460	460	NM 080601 NM 014369	BDP1	7	Under Review Cancer Panel
15	PTPN5		565	565	NM 032781	STEP, PTPSTEP, FLJ14427		Provisional RefSeq
16	PTPN9	<del>-</del>	593 595	593	NM 002833 NM 002831	MEG2 HCP_HCPH_SHP-1	<b>~</b>	Phagocytosis
17	PTPN6	. C . E	597	595	NM 080548 NM 080549	HPTP1C, PTP-1C, SHP-1L, SH-PTP1	ი ო	Hematopoietic cells
		· —	200				~	RAS related
18	PTPRE	8	642	642	NM 130435	PTPE, HPTPE, R. PTP-EPSILON	2	patrways; SATA signaling; activation of voltage-gated K+ channels
19	PTPN22	- 2	807	691	NM 015967 NM 012411	LYP, Lyp1, Lyp2	- 2	Primarily Lymphoid tissues. Associates with CBL
20	PTPN12		780	780	NM 002835	PTPG1, PTP-PEST		Cancer Panel

# FIGURE 3C

Bindingzyme	Gene ID	Variant	Peptide Length	Shortest	RefSeq ID	Aliases	Isoforms	Comment
21	PTPN3		913	913	NM 002829	PTPH1		Band 4.1 domain. P97 is a substrate. Regulated by adaptor protein 14-
22	PTPN4		926	926	NM_002830	PTPMEG, PTPMEG1		3-3 beta. Band 4.1 domain
23	PTPRN		626	626	NM 002846	IA2, IA-2, ICA512, R- PTP-N, IA-2/PTP		Diabetes
24	PTPRN2	7 7	1015 998	. 986	NM 002847 NM 130842	IAR, ICAAR, PTPRP, PHOGRIN,	- 2	Diabetes
		က	986		NM 130843	IAR PTPRP	က	
25	PTPRH		1118	1118	NM 002842	SAP-1		Cancer Panel
26	PTPN21		1174	1174	NM 007039	PTPD1, PTPRL10		BMX/ETK interaction
27	PTPN14		1187	1187	NM 005401	PEZ, PTP36		Band 4.1 domain
28	PTPRJ		1337	1337	NM_002843	DEP1, SCC1, CD148, HPTPeta, R- PTP-ETA		(-) regulator of T- cell signalling
		- 2	1436 1440		NM 133178 NM 133177	FMI, PTP, PCP-2, PTP-J, PTPRO,	- 0	MAM domain.
59	PTPRU	က	1446	1436	NM 005704	PTPU2, GLEPP1, PTP-PI, PTPPSI, hPTP-J, R-PTP-PSI,	ო	development. Regulated by PMA in Jurkat cells.
30	PTPRK		1440	1440	NM 002844	pi K-r i r-rsi R-PTP-kappa		MAM domain. Candidate for
31	PTPRG		1445	1445	NM 002841	PTPG, HPTPG, RPTPG, R-PTP- GAMMA		Cancer Panel. CAH domain.

## FIGURE 3D

Comment	MAM domain	MAM domain. Central nervous system.	Neuron growth, axon guidance	Axonogenesis and nerve repair.	Predicted RefSeq	Diabetes	Implicated in cell adhesion, neurite growth, and neuronal	Potential role in Fas-mediated programmed cell death; Rho signaling pathway
Isoforms		- 2	− 0 m 4	- 0 m 4		- 2		- N W 4
Aliases	RPTPM, RPTPU, PTPRL1, hR-PTPu, R-PTP-MU	RPTPrho, KIAA0283	HPTP, PTPD, HPTPD, HPTP- DELTA, R-PTP- DELTA	PTPSIGMA	HDPTP, HD-PTP, KIAA1471, DKFZP564F0923	LAR	PTPB, HPTPB, HPTP-BETA, R- PTP-BETA	PNP1, FAP-1, PTP1E, PTPL1, PTPLE, PTP-BL, PTP-BAS
RefSeq ID	NM 002845	NM 133170 NM 007050	NM 130391 NM 130392 NM 130393 NM 130393	NM 002850 NM 130854 NM 130853 NM 130855	NM 015466	NM 002840 NM 130440	NM_002837	NM 080683 NM 006264 NM 080684 NM 080685
Shortest	1452	1463	1501	1501	1636	1888	1997	2294
Peptide Length	1452	1463	1912 1899 1903 1501	1948 1910 1501	1636	1897 1888	1997	2485 2466 2294 2490
Variant		7 2	- 0 m 4	- 0 m 4		- 2		- C & 4
Gene ID	PTPRM	PTPRT	PTPRD	PTPRS	PTPN23	PTPRF	PTPRB	PTPN13
Bindingzyme	32	33	34	35	36	37	38	39

FIGURE 4A
Candidate PTPS

Phosphatase	Genbank accession number	Coding sequence (bp)	Isolated from	MW wildtype (KDa)	MW fusion proteins GST / MBP	Mutant 1	Mutant 2	Double Mutant
He PTP variant 1	NM 002832	1,083 bp	Jurkat	40.5	66.5 / 82.5	D257A	Q335A	D257A Q335A
He PTP variant 2	NM 080588	1,200 bp	Jurkat	45.0	71.0 / 87.0	D296A	Q374A	D296A Q374A
MEG2	NM 002833	1,782 bp	Jurkat	0.89	94.0 / 110.0	D470A	Q559A	D470A Q559A
PTEN	NM 000314	1,212 bp	Jurkat	47.2	73.2 / 89.2	D92A	C124A	D92A C124A
SHP2 variant 1	NM 002834	1,782 bp	Jurkat	68.1	94.1 / 110.2	D425A	Q526A	D425A Q526A
SHP2 variant 2	NM 080601	1,383 bp	Jurkat	52.8	78.8 / 94.8	D425A		D425A —
TCPTP variant 1	NM 002828	1,248 bp	Jurkat	48.5	74.5 / 90.5	D182A	Q260A	D182A Q260A
PEST*	NM 002835	1,041 bp	K562	40.6	66.6 / 82.6	D199A	Q278A	D199A Q278A
PTP1B	M33689	1,308 bp	K562	50.0	76.0 / 92.0	D181A	Q262A	D181A Q262A

FIGURE 4B
PCR and Mutagenesis Primers

Phosphatase	PCR forward	PCR reverse	Mutant 1	Mutant 2
HePTP	GAC GGA TCC ATG GTC CAA	CAG GTC GAC TCA GGG GCT	G GCC TGG CCA <u>GCC</u> CAT	A GGG GGG ATG ATC <u>GCG</u> ACG GCA
Variant 1	GCC CAT GGG	GGG TTC CTC	CAG ACA CCA	GAG CAG T
HePTP	GAC GGA TCC ATG GGA GCC	CAG GTC GAC TCA GGG GCT	G GCC TGG CCA <u>GCC</u> CAT	A GGG GGG ATG ATC <u>GCG</u> ACG GCA
variant 2	TCC TTC TGG	GGG TTC CTC A	CAG ACA CCA	GAG CAG T
MEG2	ATA GAA TTC ATG GAG CCC	ATA TCT AGA TTA CTG ACT	TTG AGC TGG CCA <u>GCC</u> TAT	G GCC TTC AGC ATC <u>GCG</u> ACC CCT
	GCG ACC GC	CTC CAC GGC CAG	GGT GTC CCT TC	GAG CAG T
PTEN	GAC GAA TTC ATG ACA GCC	CAG TCT AGA TCA GAC TTT	CA CAA TAT CCT TTT GAA	T CAT GTT GCA GCA ATT CAC GCT
	ATC ATC AAA GAG	TGT AAT TTG TGT ATG C	GCC CAT AAC CCA CCA CAG	AAA GCT GGA AAG GGA CG
SHP2	GAC GAA TTC ATG ACA TCG	CAG TCT AGA TCA TCT GAA	G ACC TGG CCG <u>GCC</u> CAC	C CAG CAT TAT ATT GAA ACA CTA
variant 1	CGG AGA TGG	ACT TTT CTG CTG TTG	GGC GTG C	GCG CGC AGG ATT GAA GAA GAG
SHP2	GAC GAA TTC ATG ACA TCG	CAG TCT AGA TCA CCT GCA	G ACC TGG CCG <u>GCC</u> CAC	
variant 2	CGG AGA TGG	GTG CAC CAC	GGC GTG C	
TCPTP	GAC GAA TTC ATG CCC ACC	CA GGT CGA CAT TGT TTA	T TAT ACT ACC TGG CCA <u>GCT</u>	AC CGA ATG GGT CTT ATT <u>CCG</u> ACC
variant 1	ACC ATC GAG	TAG GGC ATT TTG CT G	TTT GGA GTC CCT GAA T	CCA GAT CAA CTG AG
PEST	GAC GGA TCC ATG GAG CAA	CAG GTC GAC TCA TTC AAC	TAT GTG AAC TGG CCVA <u>GCC</u>	CA CAA AGG CAT TCT GCA GTA <u>GCA</u>
	GTC GAG ATC CTG	AAG GCA ACT GCG GG	CAT GAT GTT CCT TCA TC	ACA AAG GAG CAA TAT GAA CT
PTP1B	GAC GGA TCC ATG GAG ATG	CAG GTC GAC CTA TGT GTT	T ACC ACA TGG CCT <u>GCC</u> TTT	G ATG GGG CTG ATC <u>GCG</u> ACA GCC
	GAA AAG GAG TTC G	GCT GTT GAA CAG G	GGA GTC CCT G	GAC CAG C

1. Profiling Panel: Different Bindingzyme each well; Duplicate Plates. Lysates from cancer and normal cells are incubated with Profiling Panel to capture Phosphoproteins.

### Normal counterpart Cancer cell

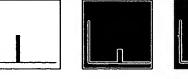


1 different Bindingzyme per well "Profiling Panel"

Marked wells indicate differences between samples

2. Identify Informative Bindingzymes:

Using MALDI-TOF MS, well-to-well comparisons of captured phosphoproteins are done to find those Bindingzymes that detect a difference between samples. (Spectra are simplified to convey concept.)



Normal Cell Profiles







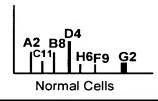
Cancer Cell **Profiles** 

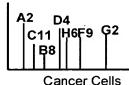
No change

Up-regulated Down-regulated

3. Screening Assay is Created:

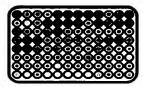
Informative Bindingzymes are combined to create the Screening Assay, which can detect all of the differences found by the Profiling Panel, Numbers above each peak refer to the original Profiling Panel position.





4. Screening Plate: Different lysate, same Informative Bindingzymes each well:

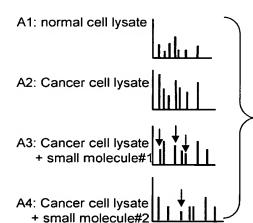
Lysates from cancer cells exposed to different compounds from a small molecule library are incubated with Screening Plates where each well contains the Screening Assay (identical set of Informative Bindingzymes).



7 Informative Bindingzymes per well "Screening Plate"

5. Drug Candidates are Identified:

Eluted phosphoproteins are analyzed by MALDI-TOF MS. Any compound that changes the cancer profile toward the normal cell profile is a drug candidate.



Identify drug candidates that shift the cancer profile towards normal (as indicated)